# Pharmaceutical Approval Update

**Kunj Gohil, PharmD, RPh**

## Palbociclib (Ibrance)

**Manufacturer:** Pfizer Inc., New York, New York

**Date of Approval:** February 3, 2015

**Indication:** Palbociclib is indicated, in combination with letrozole, for the treatment of postmenopausal women with estrogen receptor–positive, human epidermal growth factor receptor 2–negative advanced breast cancer as initial endocrine-based therapy for their metastatic disease.

Kunj Gohil, PharmD, RPh

**Drug Class:** Palbociclib is an inhibitor of cyclin-dependent kinase (CDK) 4 and 6.

**Uniqueness of Drug:** Cyclin D1 and CDK 4/6 are downstream of signaling pathways that lead to cellular proliferation. Treatment of breast cancer cell lines with the combination of palbociclib and anti-estrogens leads to decreased retinoblastoma protein phosphorylation, resulting in reduced E2F expression and signaling and increased growth arrest compared to treatment with either drug alone.

**Warnings and Precautions:**

***Neutropenia.*** Monitor complete blood count prior to starting palbociclib therapy and at the beginning of each cycle, as well as on day 14 of the first two cycles and as clinically indicated. Dose interruption, dose reduction, or a delay in starting treatment cycles is recommended for patients who develop grade 3 or 4 neutropenia.

***Infections.*** Monitor patients for signs and symptoms of infection and treat as medically appropriate.

***Pulmonary embolism.*** Monitor patients for signs and symptoms of pulmonary embolism and treat as medically appropriate.

***Embryo-fetal toxicity.*** Advise females of reproductive potential to use effective contraception during therapy with palbociclib and for at least two weeks after the last dose.

**Dosage and Administration:** The recommended dose of Ibrance is a 125-mg capsule taken orally once daily for 21 consecutive days followed by seven days off treatment, comprising a complete cycle of 28 days.

**Commentary:** With millions of patients affected by breast cancer, there is a need for efficacious therapies targeting specific types of the disease. Ibrance provides certain postmenopausal women with a novel option for their metastatic breast cancer. This drug received a breakthrough therapy designation and priority review, allowing its approval two months ahead of the original Prescription Drug User Fee Act (PDUFA) goal date; it was also reviewed under the accelerated approval program, allowing the use of a surrogate endpoint associated with clinical benefits.

**Sources:** Ibrance prescribing information and www.fda.gov

*Dr. Gohil is Central Services Manager with Medical Services at MediMedia Managed Markets in Yardley, Pennsylvania. His email address is kgohil@medimedia.com.*

## Secukinumab (Cosentyx)

**Manufacturer:** Novartis Pharmaceuticals Corporation, East Hanover, New Jersey

**Date of Approval:** January 21, 2015

**Indication:** Secukinumab is indicated for the treatment of moderate-to-severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy.

**Drug Class:** Secukinumab is a human immunoglobulin G1 monoclonal antibody that selectively binds to the interleukin-17A (IL-17A) cytokine and inhibits its interaction with the IL-17 receptor.

**Uniqueness of Drug:** IL-17A is a naturally occurring cytokine that is involved in normal inflammatory and immune responses; elevated levels of IL-17A are found in psoriatic plaques. Secukinumab inhibits the release of proinflammatory cytokines and chemokines.

**Warnings and Precautions:**

***Infections.*** Exercise caution when considering the use of secukinumab in patients with a chronic infection or a history of recurrent infection. Instruct patients to seek medical advice if signs or symptoms suggestive of an infection occur. If a patient develops a serious infection, he or she should be closely monitored and secukinumab should be discontinued until the infection resolves.

***Pretreatment evaluation for tuberculosis (TB).*** Evaluate patients for TB infection prior to initiating treatment with secukinumab. Do not administer secukinumab to patients with active TB infection. Initiate treatment of latent TB prior to administering secukinumab. Consider anti-TB therapy prior to initiation of secukinumab in patients with a history of latent or active TB in whom an adequate course of treatment cannot be confirmed. Patients receiving secukinumab should be monitored closely for signs and symptoms of active TB during and after treatment.

***Exacerbations of Crohn's disease.*** Patients who are treated with secukinumab and have active Crohn's disease should be monitored closely.

***Hypersensitivity reactions.*** If an anaphylactic or other serious allergic reaction occurs, administration of secukinumab should be discontinued immediately and appropriate therapy initiated.

***Risk of hypersensitivity in latex-sensitive individuals.*** The removable cap of the Cosentyx Sensoready pen and the Cosentyx prefilled syringe contain natural rubber latex, which may cause an allergic reaction in latex-sensitive individuals.

***Vaccinations.*** Prior to initiating therapy with secukinumab, consider completion of all age-appropriate immunizations according to current immunization guidelines. Patients treated with secukinumab should not receive live vaccines.

**Dosage and Administration:** The recommended dose is 300 mg by subcutaneous injection at weeks 0, 1, 2, 3, and 4, followed by 300 mg every four weeks. Each 300-mg dose is given as two subcutaneous injections of 150 mg.

**Commentary:** Plaque psoriasis is a significant skin condi-

tion that causes irritation and discomfort for patients. Cosentyx offers patients eligible for systemic therapies another alternative for treating this disease. Because the drug's mechanism of action affects the immune system, patients may be at greater risk for infections, so caution should be exercised in patients with a history of infections.

**Sources:** Cosentyx prescribing information and www.fda.gov

## Meningococcal Group B Vaccine (Bexsero)

**Manufacturer:** Novartis Vaccines and Diagnostics Inc., Cambridge, Massachusetts

**Date of Approval:** January 23, 2015

**Indication:** Bexsero is indicated for active immunization to prevent invasive disease caused by *Neisseria meningitidis* serogroup B. It is approved for use in individuals 10 through 25 years of age.

**Drug Class:** Vaccine

**Uniqueness of Drug:** Use of Bexsero leads to the production of antibodies against certain proteins found on the surface of the meningococci bacterium. Protection against invasive meningococcal disease is conferred mainly by complement-mediated, antibody-dependent killing of *N. meningitidis*.

**Warnings and Precautions:**

***Preventing and managing allergic reactions.*** Appropriate observation and medical treatment should always be readily available in case of an anaphylactic event following the administration of the vaccine.

***Syncope.*** Fainting can occur in association with administration of the vaccine. Ensure procedures are in place to avoid injury from falling associated with syncope.

***Latex.*** The tip caps of the prefilled syringes contain natural rubber latex that may cause allergic reactions in latex-sensitive individuals.

***Limitation of vaccine effectiveness.*** Bexsero may not protect all vaccine recipients and may not provide protection against all meningococcal serogroup B strains.

***Altered immunocompetence.*** Individuals with altered immunocompetence may have reduced immune responses to this vaccine.

**Dosage and Administration:** Administer two doses (0.5 mL each) intramuscularly at least one month apart.

**Commentary:** Meningitis is a life-threatening disease that infects the bloodstream and can affect the spinal cord and the lining around the brain. Bexsero is the second vaccine approved to prevent invasive meningococcal disease caused by *N. meningitidis* serogroup B. Prior to the approval of these vaccines, traditional vaccines protected recipients against only four of the five serogroups. Bexsero was approved through the FDA's accelerated approval pathway, which will require Novartis to conduct additional studies to verify the vaccine's effectiveness. The FDA also granted a breakthrough designation to expedite the development and review of this therapy.

**Sources:** Bexsero prescribing information and www.fda.gov

## Lenvatinib (Lenvima)

**Manufacturer:** Eisai, Inc., Woodcliff Lake, New Jersey

**Date of Approval:** February 13, 2015

**Indication:** Lenvima is indicated for the treatment of patients with locally recurrent or metastatic, progressive, radioactive iodine-refractory differentiated thyroid cancer (DTC).

**Drug Class:** Lenvatinib is a kinase inhibitor that inhibits the activities of specific growth factors.

**Uniqueness of Drug:** As a receptor tyrosine kinase (RTK) inhibitor, lenvatinib inhibits specific vascular endothelial growth factor receptors, fibroblast growth factor receptors, platelet-derived growth factor receptor alpha, KIT, and RET. Some of these factors have been implicated in angiogenesis, tumor growth, and cancer progression in addition to their normal cellular functions.

**Warnings and Precautions:**

***Hypertension.*** Control blood pressure prior to treatment with lenvatinib. Monitor blood pressure after one week, then every two weeks for the first two months, and then at least monthly thereafter during treatment. Withhold lenvatinib for grade 3 hypertension despite optimal antihypertensive therapy; resume at a reduced dose when hypertension is controlled at grade 2 or lower. Discontinue lenvatinib for life-threatening hypertension.

***Cardiac dysfunction.*** Monitor patients for clinical symptoms or signs of cardiac decompensation. Withhold lenvatinib for development of grade 3 cardiac dysfunction until it improves to grade 0 or 1 or baseline. Either resume at a reduced dose or discontinue lenvatinib depending on the severity and persistence of cardiac dysfunction. Discontinue lenvatinib for grade 4 cardiac dysfunction.

***Arterial thromboembolic events.*** Discontinue lenvatinib following an arterial thrombotic event. The safety of resuming lenvatinib after an arterial thromboembolic event has not been established.

***Hepatotoxicity.*** Monitor liver function before initiation of lenvatinib, then every two weeks for the first two months, and at least monthly thereafter during treatment. Withhold lenvatinib for the development of grade 3 or greater liver impairment until it is resolved to grade 0 to 1 or baseline. Either resume at a reduced dose or discontinue lenvatinib depending on the severity and persistence of hepatotoxicity. Discontinue lenvatinib for hepatic failure.

***Proteinuria.*** Monitor for proteinuria before initiation of treatment and periodically throughout treatment. Withhold lenvatinib if tests show 2 g or more of proteinuria in 24 hours and resume at a reduced dose when proteinuria is less than 2 g in 24 hours. Discontinue lenvatinib for nephrotic syndrome.

***Renal failure and impairment.*** Withhold lenvatinib for development of grade 3 or 4 renal failure or impairment until it is resolved to grade 0 to 1 or baseline. Either resume at a reduced dose or discontinue lenvatinib depending on the severity and persistence of renal impairment.

***Gastrointestinal (GI) perforation and fistula formation.*** Discontinue lenvatinib in patients who develop GI perforation or life-threatening fistula.

***QT interval prolongation.*** Monitor and correct electrolyte abnormalities in all patients. Withhold lenvatinib for the development of grade 3 or greater QT interval prolongation. Resume lenvatinib at a reduced dose when QT prolongation resolves to grade 0 or 1 or baseline.

***Hypocalcemia.*** Monitor blood calcium levels at least monthly and replace calcium as necessary during lenvatinib

*continued on page 287*

*continued from page 252*

treatment. Interrupt and adjust lenvatinib dosing as necessary depending on severity, presence of electrocardiogram changes, and persistence of hypocalcemia.

***Reversible posterior leukoencephalopathy syndrome (RPLS).*** Confirm the diagnosis of RPLS with magnetic resonance imaging. Withhold for RPLS until fully resolved. Upon resolution, resume at a reduced dose or discontinue lenvatinib depending on the severity and persistence of neurological symptoms.

***Hemorrhagic events.*** Withhold lenvatinib for the development of grade 3 hemorrhage until resolved to grade 0 to 1. Either resume at a reduced dose or discontinue lenvatinib depending on the severity and persistence of hemorrhage. Discontinue lenvatinib in patients who experience grade 4 hemorrhage.

***Impairment of thyroid stimulating hormone (TSH) suppression.*** Monitor TSH levels monthly and adjust thyroid replacement medication as needed in patients with DTC.

***Embryo-fetal toxicity.*** Advise females of reproductive potential to use effective contraception during treatment with lenvatinib and for at least two weeks following completion of therapy.

**Dosage and Administration:** The recommended daily dose of Lenvima is 24 mg (two 10-mg capsules and one 4-mg capsule) taken orally once daily. Continue Lenvima until disease progression or until unacceptable toxicity occurs.

**Commentary:** DTC is the most common cancer that affects the thyroid gland in the neck. This cancerous growth interferes with the body's natural ability to regulate metabolism. The approval of Lenvima will give patients who are refractory to conventional therapies an alternative to slow the progression of DTC. A priority review allowed Lenvima's approval approximately two months ahead of the original PDUFA goal date. Lenvima was also granted orphan drug status because it treats a rare disease.

**Sources:** Lenvima prescribing information and www.fda.gov ■